AMENDMENTS

IN THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Withdrawn) A calcium channel blocker compound having at least one of the following characteristics:

a. the compound is metabolized both by CYP450 and by a non-oxidative metabolic enzyme or system of enzymes;

b. the compound has a short (up to four (4) hours) non-oxidative metabolic half-life;

c. the compound contains a hydrolysable bond that can be cleaved non-oxidatively by hydrolytic enzymes;

d. the primary metabolites of the compound result from the non-oxidative metabolism of the compound;

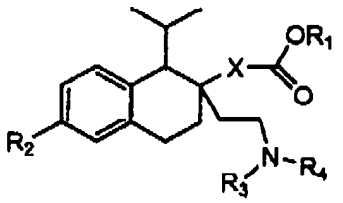
e. the primary metabolites are soluble in water at physiological pH;

f. the primary metabolites have negligible inhibitory activity at the IK_R (HERG) channel at normal therapeutic concentration of the parent drug in plasma;

g. the compound, as well as the metabolites thereof, does not cause metabolic DDI when co-administered with other drugs; and

h. the compound, as well as metabolites thereof, does not elevate LFT values when administered alone.

2. (Withdrawn) The compound, according to claim 1, having the following structure:



wherein:

X=a bond, $(CH_2)_n$, O, S, or $O(CH_2)_n$,

wherein n=1-6;

R_1=C_{1-6} alkyl, optionally substituted with OH or NH_2;

R_2=F or $COOR_5$,

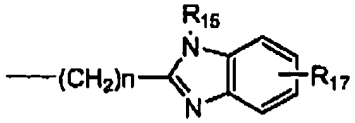
wherein R_5 is C_{1-6} alkyl, optionally substituted with OH or NH_2;

R_3=CH_3 or $(CH_2)_n$-$COOR_6$,

wherein n=1-6 and R_6 is C_{1-6} alkyl, optionally substituted with OH or NH_2;

PAGE 3/22 * RCVD AT 5/6/2005 4:11:55 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/24 * DNIS:2730686 * CSID:3129130002 * DURATION (mm-ss):04-50

R_4=$(CH_2)_n$-COR_7R_8, -$(CH_2)_n$-$R_{10}R_{11}$ or



R_7=O, NH, or NR_9,

R_8=optionally substituted aryl or heterocycle,

R_9=C_{1-6} alkyl,

R_{10}=O, S, SO, SO_2, NH, or NR_{12} ~~or $N(CH_2)_mCOOR_{13}$~~,

R_{11}=aryl or heterocyclyl optionally substituted with $(CH_2)_nCOOR_{14}$,

R_{12}=C_{1-6} alkyl, optionally substituted with OH or NH_2,

R_{13}=C_{1-6} alkyl, optionally substituted with OH or NH_2,

R_{14}=C_{1-6} alkyl, optionally substituted with OH or NH_2,

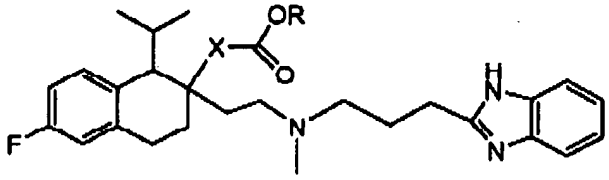
R_{15}=$(CH_2)_nCOOR_{16}$,

R_{16}=C_{1-6} alkyl, optionally substituted with OH or NH_2,

R_{17}=not present or $COOR_{18}$ wherein R_{18} is C_{1-6} alkyl, optionally substituted with OH or NH_2, and

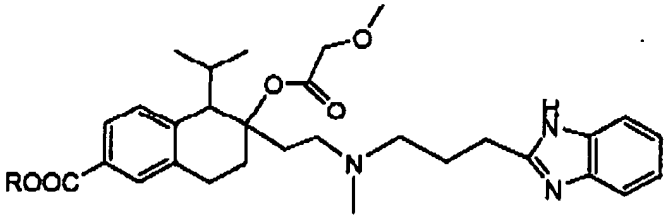
wherein n=1-6.

3. (Withdrawn) The compound, according to claim 2, having a formula selected from the group consisting of:



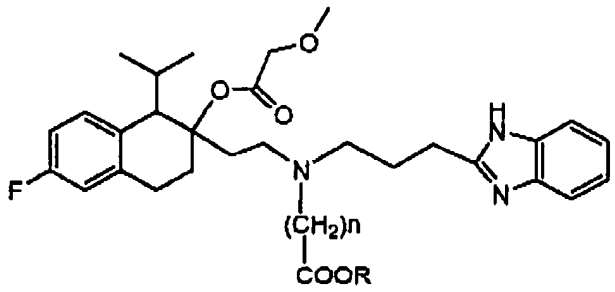
X=bond, CH_2, or OCH_2

R=lower alkyl optionally substituted OH or NH_2;



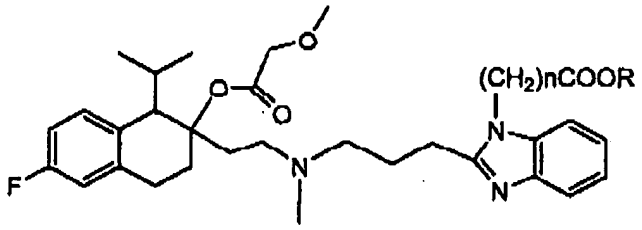
R=lower alkyl optionally substituted by OH or NH_2;

PAGE 4/22 * RCVD AT 5/6/2005 4:11:55 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/24 * DNIS:2730686 * CSID:3129130002 * DURATION (mm-ss):04-50



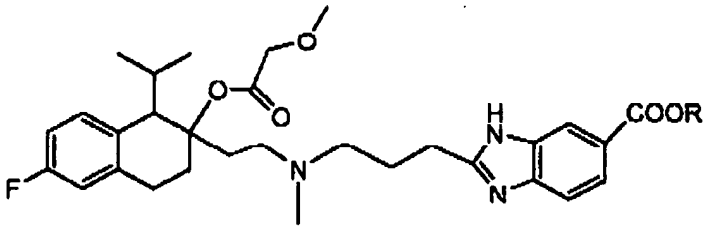
n=1 to 3

R=lower alkyl optionally substituted by OH or NH_2;

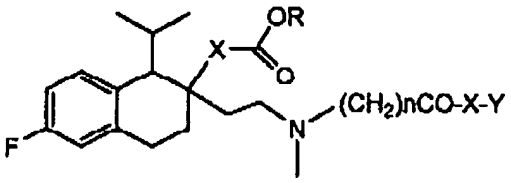


n=1 to 3

R=lower alkyl optionally substituted by OH or NH_2;

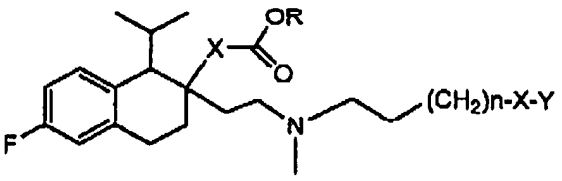


R=lower alkyl optionally substituted by OH or NH_2;



n=1 to 3 X=O, NH, NR where R is lower alkyl

Y=optionally substituted aryl or heterocyclyl; and



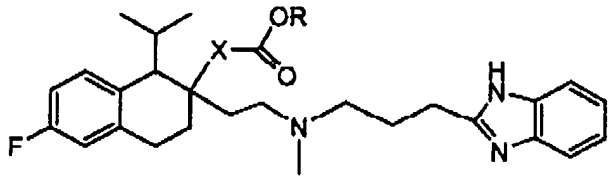
n=0 to 2

PAGE 5/22 * RCVD AT 5/6/2005 4:11:55 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/24 * DNIS:2730686 * CSID:3129130002 * DURATION (mm-ss):04-50

X=O, S, SO, SO_2, NH NR or $N(CH_2)_mCOOH$ where m is 0 or 2

Y=aryl or heterocyclyl substituted with $(CH_2)_mCOOH$ where m is 0 to 2.

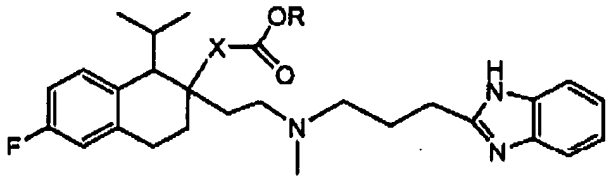
4. (Withdrawn) The compound, according to claim 3, having the following structure:



X=bond, CH_2, or OCH_2

R=lower alkyl optionally substituted OH or NH_2.

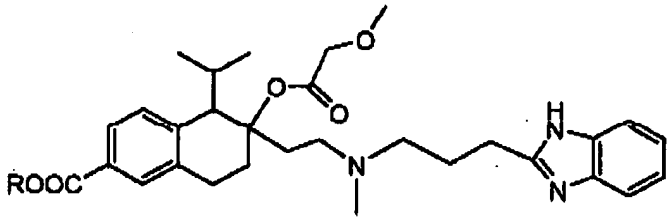
5. (Withdrawn) The compound, according to claim 3, having the following structure:



X=bond, CH_2, or OCH_2

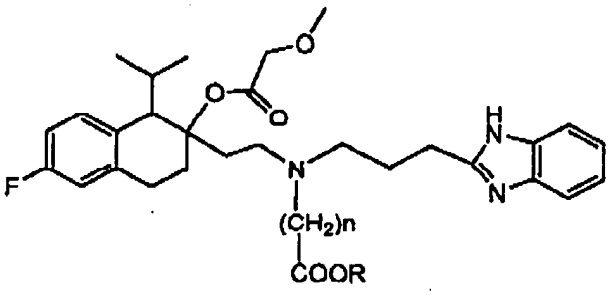
R=lower alkyl optionally substituted OH or NH_2.

6. (Withdrawn) The compound, according to claim 3, having the following structure:



R=lower alkyl optionally substituted by OH or NH_2.

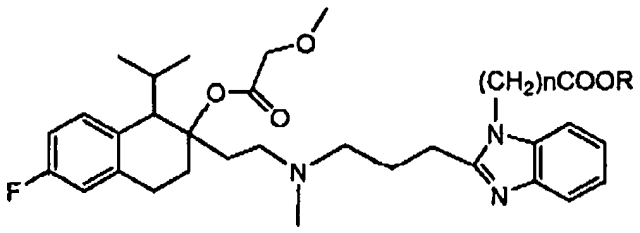
7. (Withdrawn) The compound, according to claim 3, having the following structure:



n=1 to 3

R=lower alkyl optionally substituted by OH or NH_2.

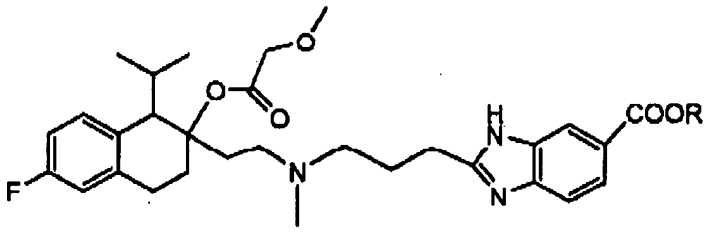
8. (Withdrawn) The compound, according to claim 3, having the following structure:



n=1 to 3

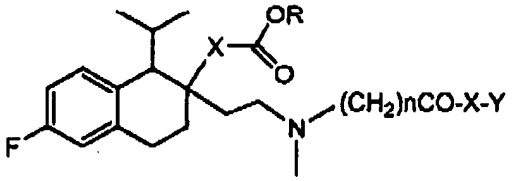
R=lower alkyl optionally substituted by OH or NH_2.

9. (Withdrawn) The compound, according to claim 3, having the following structure:



R=lower alkyl optionally substituted by OH or NH_2.

10. (Withdrawn) The compound, according to claim 3, having the following structure:

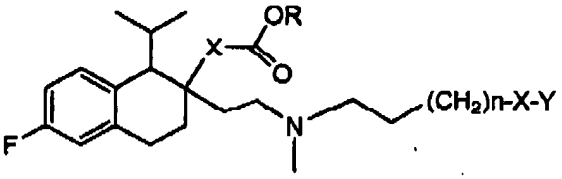


n=1 to 3

X=O, NH, NR where R is lower alkyl

Y=optionally substituted aryl or heterocyclyl.

11. (Withdrawn) The compound, according to claim 3, having the following structure:



n=0 to 2

X=O, S, SO, SO_2, NH NR or $N(CH_2)_mCOOH$ where m is 0 or 2

PAGE 7/22 * RCVD AT 5/6/2005 4:11:55 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/24 * DNIS:2730686 * CSID:3129130002 * DURATION (mm-ss):04-50

Y=aryl or heterocyclyl substituted with $(CH_2)_mCOOH$ where m is 0 to 2.

12. (Withdrawn) A pharmaceutical composition comprising a calcium channel blocker compound having at least one of the following characteristics:

a. the compound is metabolized both by CYP450 and by a non-oxidative metabolic enzyme or system of enzymes;

b. the compound has a short (up to four (4) hours) non-oxidative metabolic half-life;

c. the compound contains a hydrolysable bond that can be cleaved non-oxidatively by hydrolytic enzymes;

d. the primary metabolites of the compound result from the non-oxidative metabolism of the compound;

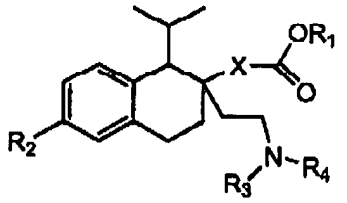
e. the primary metabolites are soluble in water at physiological pH;

f. the primary metabolites have negligible inhibitory activity at the IK_R (HERG) channel at normal therapeutic concentration of the parent drug in plasma;

g. the compound, as well as the metabolites thereof, does not cause metabolic DDI when co-administered with other drugs; and

h. the compound, as well as metabolites thereof, does not elevate LFT values when administered alone; wherein said composition further comprises a pharmaceutical carrier.

13. (Withdrawn) The pharmaceutical composition, according to claim 12, wherein said compound has the following structure:



wherein:

X=a bond, $(CH_2)_n$, O, S, or $O(CH_2)_n$,

wherein n=1-6;

R_1=C_{1-6} alkyl, optionally substituted with OH or NH_2;

R_2=F or $COOR_5$,

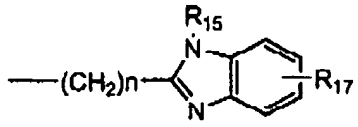
wherein R_5 is C_{1-6} alkyl, optionally substituted with OH or NH_2;

R_3=CH_3 or $(CH_2)_n$–$COOR_6$,

wherein n=1-6 and R_6 is C_{1-6} alkyl, optionally substituted with OH or NH_2;

R_4=$(CH_2)_n$–COR_7R_8, –$(CH_2)_n$–$R_{10}R_{11}$ or

PAGE 8/22 * RCVD AT 5/6/2005 4:11:55 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/24 * DNIS:2730686 * CSID:3129130002 * DURATION (mm-ss):04-50



R_7=O, NH, or NR_9,

R_8=optionally substituted aryl or heterocycle,

R_9=C_{1-6} alkyl,

R_{10}=O, S, SO, SO_2, NH, or NR_{12} ~~or $N(CH_2)_mCOOR_{13}$~~,

R_{11}=aryl or heterocyclyl optionally substituted with $(CH_2)_nCOOR_{14}$,

R_{12}=C_{1-6} alkyl, optionally substituted with OH or NH_2,

R_{13}=C_{1-6} alkyl, optionally substituted with OH or NH_2,

R_{14}=C_{1-6} alkyl, optionally substituted with OH or NH_2,

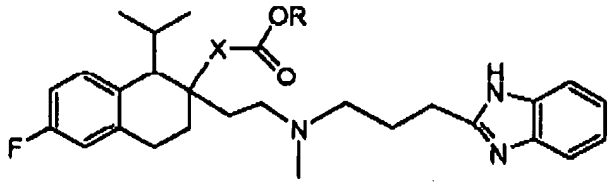
R_{15}=$(CH_2)_nCOOR_{16}$,

R_{16}=C_{1-6} alkyl, optionally substituted with OH or NH_2,

R_{17}=not present or $COOR_{18}$ wherein R_{18} is C_{1-6} alkyl, optionally substituted with OH or NH_2, and

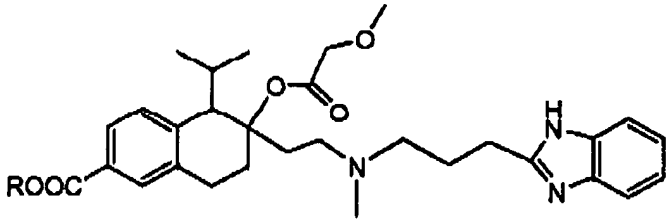
wherein n=1-6.

14. (Withdrawn) The composition, according to claim 13, comprising a compound having a formula selected from the group consisting of:



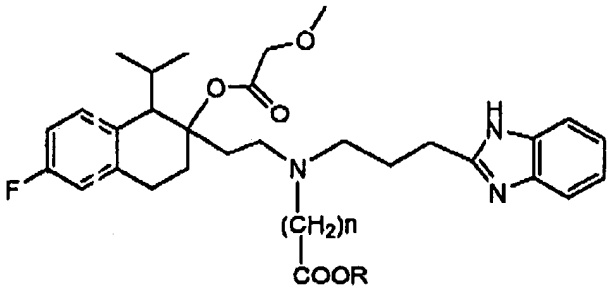
X=bond, CH_2, or OCH_2

R=lower alkyl optionally substituted OH or NH_2;



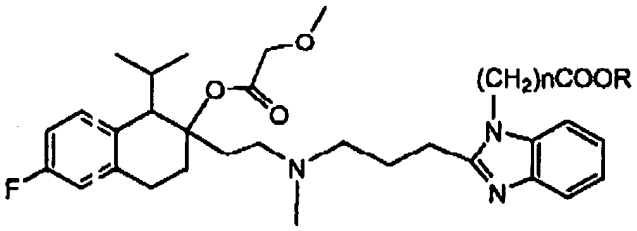
R=lower alkyl optionally substituted by OH or NH_2;

PAGE 9/22 * RCVD AT 5/6/2005 4:11:55 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/24 * DNIS:2730686 * CSID:3129130002 * DURATION (mm-ss):04-50



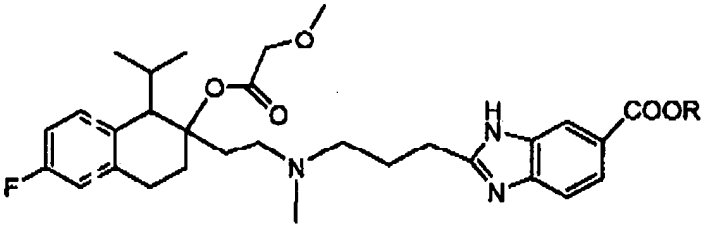
n=1 to 3

R=lower alkyl optionally substituted by OH or NH_2;

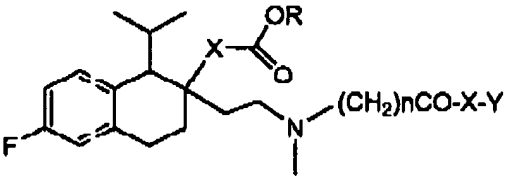


n=1 to 3

R=lower alkyl optionally substituted by OH or NH_2;

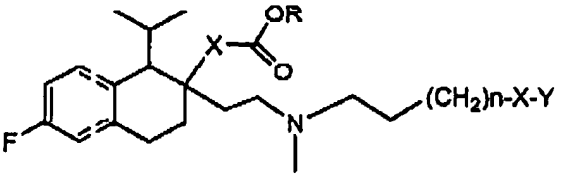


R=lower alkyl optionally substituted by OH or NH_2;



n=1 to 3 X=O, NH, NR where R is lower alkyl

Y=optionally substituted aryl or heterocyclyl; and



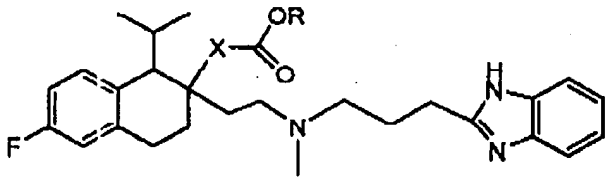
n=0 to 2

PAGE 10/22 * RCVD AT 5/6/2005 4:11:55 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/24 * DNIS:2730686 * CSID:3129130002 * DURATION (mm-ss):04-50

X=O, S, SO, SO_2, NH NR or $N(CH_2)_mCOOH$ where m is 0 or 2

Y=aryl or heterocyclyl substituted with $(CH_2)_mCOOH$ where m is 0 to 2.

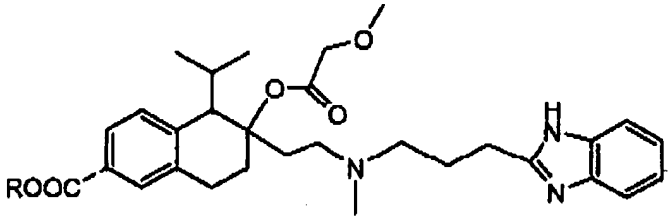
15. (Withdrawn) The compound, according to claim 14, comprising a compound having the following structure:



X=bond, CH_2, or OCH_2

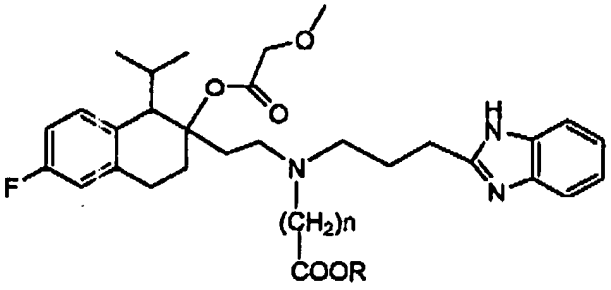
R=lower alkyl optionally substituted OH or NH_2.

16. (Withdrawn) The compound, according to claim 14, having the following structure:



R=lower alkyl optionally substituted by OH or NH_2.

17. (Withdrawn) The compound, according to claim 14, having the following structure:

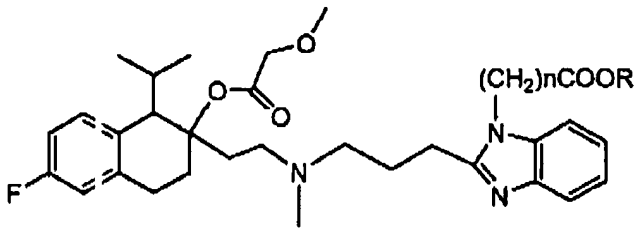


n=1 to 3

R=lower alkyl optionally substituted by OH or NH_2.

18. (Withdrawn) The compound, according to claim 14, having the following structure:

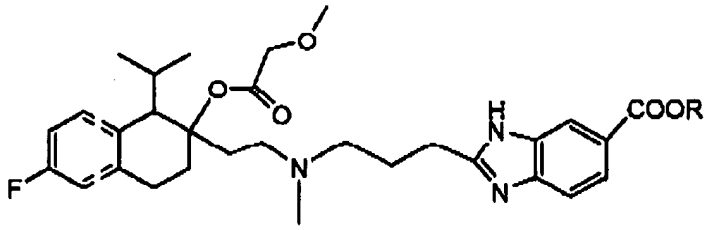
PAGE 11/22 * RCVD AT 5/6/2005 4:11:55 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/24 * DNIS:2730686 * CSID:3129130002 * DURATION (mm-ss):04-50



n=1 to 3

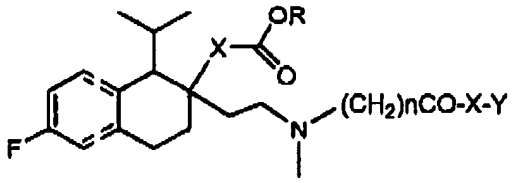
R=lower alkyl optionally substituted by OH or NH_2.

19. (Withdrawn) The compound, according to claim 14, having the following structure:



R=lower alkyl optionally substituted by OH or NH_2.

20. (Withdrawn) The compound, according to claim 14, having the following structure:

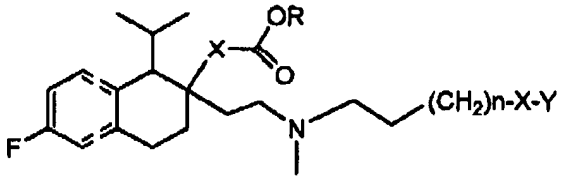


n=1 to 3

X=O, NH NR where R is lower alkyl

Y=optionally substituted aryl or heterocyclyl.

21. (Withdrawn) The compound, according to claim 14, having the following structure:



n=0 to 2

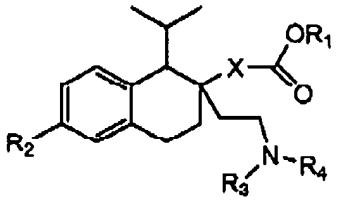
X=O, S, SO, SO_2, NH NR or $N(CH_2)_mCOOH$ where m is 0 or 2

Y=aryl or heterocyclyl substituted with $(CH_2)_mCOOH$ where m is 0 to 2.

22. (Canceled)

PAGE 12/22 * RCVD AT 5/6/2005 4:11:55 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/24 * DNIS:2730686 * CSID:3129130002 * DURATION (mm-ss):04-50

23. (Currently Amended) ~~The method, according to claim 22,~~ A method for blocking a calcium channel in a patient in need of such blocking wherein said method comprises administering to said patient a calcium channel blocking compound wherein said compound has the following structure:



wherein:

X=a bond, $(CH_2)_n$, O, S, or $O(CH_2)_n$,

wherein n=1-6;

R_1=C_{1-6} alkyl, optionally substituted with OH or NH_2;

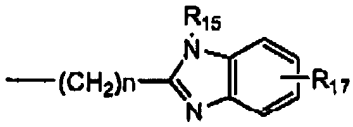
R_2=F or $COOR_5$,

wherein R_5 is C_{1-6} alkyl, optionally substituted with OH or NH_2;

R_3=CH_3 or $(CH_2)_n$-$COOR_6$,

wherein n=1-6 and R_6 is C_{1-6} alkyl, optionally substituted with OH or NH_2;

R_4=$(CH_2)_n$-COR_7R_8, -$(CH_2)_n$-$R_{10}R_{11}$ or



R_7=O, NH, or NR_9,

R_8=optionally substituted aryl or heterocycle,

R_9=C_{1-6} alkyl,

R_{10}=O, S, SO, SO_2, NH, or NR_{12} ~~or $N(CH_2)_mCOOR_{13}$~~,

R_{11}=aryl or heterocyclyl optionally substituted with $(CH_2)_nCOOR_{14}$,

R_{12}=C_{1-6} alkyl, optionally substituted with OH or NH_2,

R_{13}=C_{1-6} alkyl, optionally substituted with OH or NH_2,

R_{14}=C_{1-6} alkyl, optionally substituted with OH or NH_2,

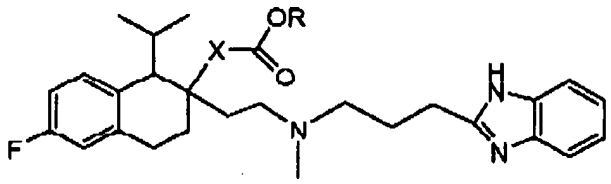
R_{15}= $(CH_2)_nCOOR_{16}$,

R_{16}=C_{1-6} alkyl, optionally substituted with OH or NH_2,

R_{17}=not present or $COOR_{18}$ wherein R_{18} is C_{1-6} alkyl, optionally substituted with OH or NH_2, and wherein n=1-6.

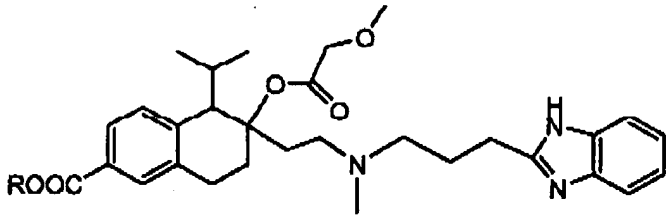
PAGE 13/22 * RCVD AT 5/6/2005 4:11:55 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/24 * DNIS:2730686 * CSID:3129130002 * DURATION (mm-ss):04-50

24. (Currently Amended) ~~The method, according to claim 23,~~ A method for blocking a calcium channel in a patient in need of such blocking wherein said method comprises administering to said patient a calcium channel blocking compound wherein said compound has a formula selected from the group consisting of:

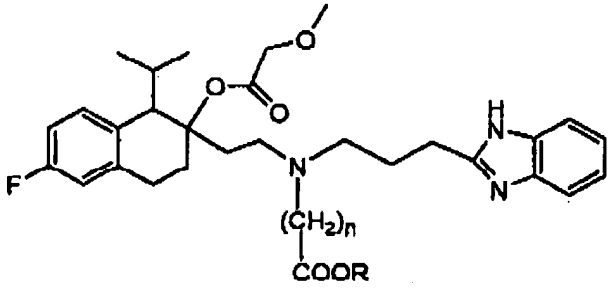


X=bond, CH_2, or OCH_2

R=lower alkyl optionally substituted OH or NH_2;

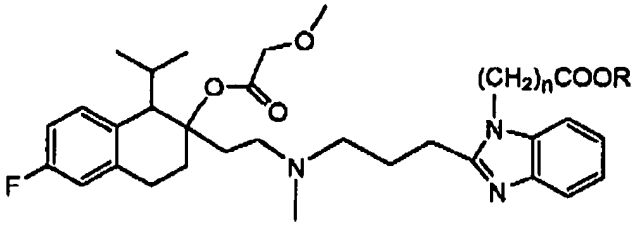


R=lower alkyl optionally substituted by OH or NH_2;



n=1 to 3

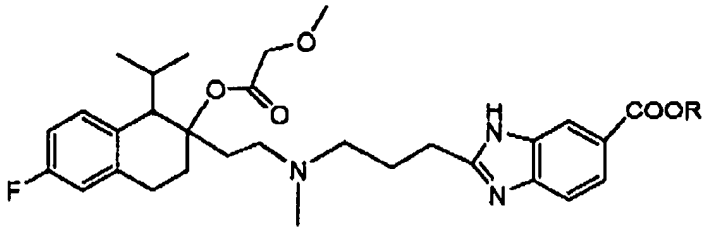
R=lower alkyl optionally substituted by OH or NH_2;



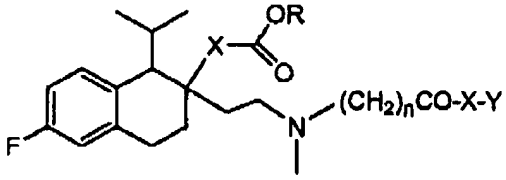
n=1 to 3

R=lower alkyl optionally substituted by OH or NH_2;

PAGE 14/22 * RCVD AT 5/6/2005 4:11:55 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/24 * DNIS:2730686 * CSID:3129130002 * DURATION (mm-ss):04-50

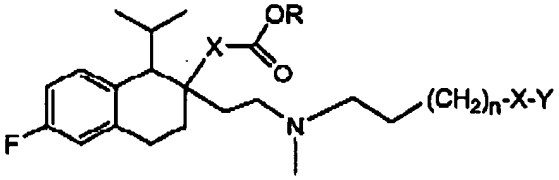


R=lower alkyl optionally substituted by OH or NH_2;



n=1 to 3 X=O, NH, NR where R is lower alkyl

Y=optionally substituted aryl or heterocyclyl; and

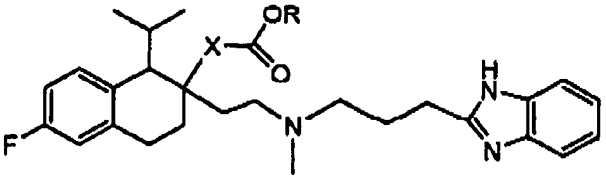


n=0 to 2

X=O, S, SO, SO_2, NH NR or $N(CH_2)_mCOOH$ where m is 0 or 2

Y=aryl or heterocyclyl substituted with $(CH_2)_mCOOH$ where m is 0 to 2.

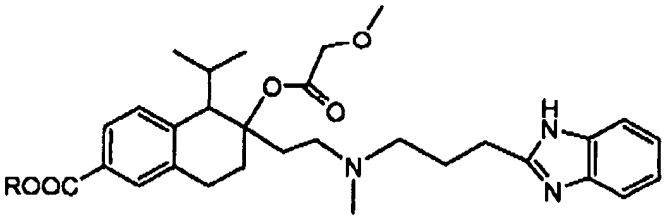
25. (Original) The compound, according to claim 24, wherein said compound has the following structure:



X=bond, CH_2, or OCH_2

R=lower alkyl optionally substituted OH or NH_2.

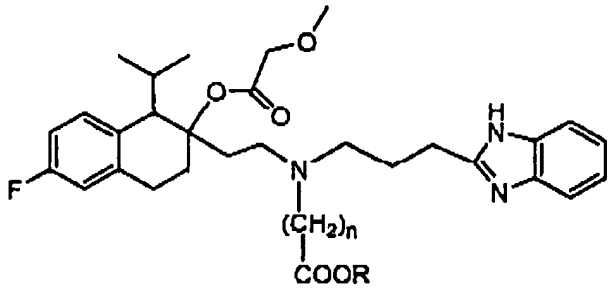
26. (Original) The compound, according to claim 24, wherein said compound has the following structure:



PAGE 15/22 * RCVD AT 5/6/2005 4:11:55 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/24 * DNIS:2730686 * CSID:3129130002 * DURATION (mm-ss):04-50

R=lower alkyl optionally substituted by OH or NH_2.

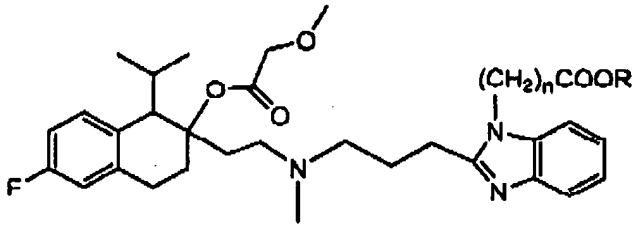
27. (Original) The compound, according to claim 24, wherein said compound has the following structure:



n=1 to 3

R=lower alkyl optionally substituted by OH or NH_2.

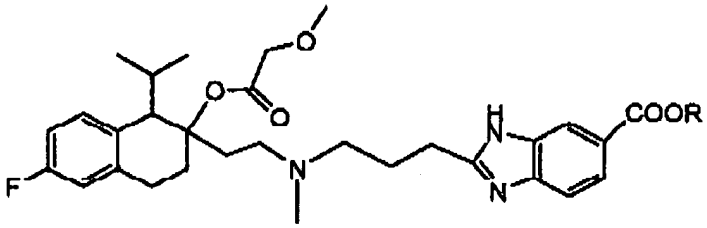
28. (Original) The compound, according to claim 24, wherein said compound has the following structure:



n=1 to 3

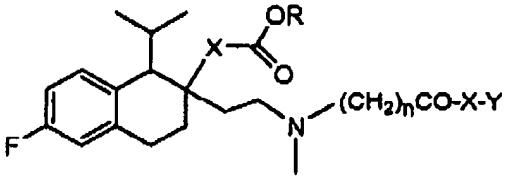
R=lower alkyl optionally substituted by OH or NH_2.

29. (Original) The compound, according to claim 24, wherein said compound has the following structure:



R=lower alkyl optionally substituted by OH or NH_2.

30. (Withdrawn) The compound, according to claim 24, wherein said compound has the following structure:



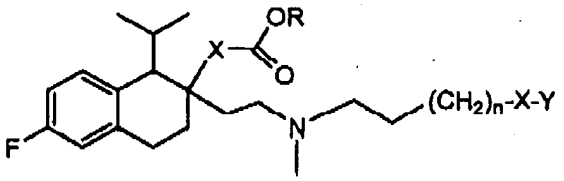
n=1 to 3

PAGE 16/22 * RCVD AT 5/6/2005 4:11:55 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/24 * DNIS:2730686 * CSID:3129130002 * DURATION (mm-ss):04-50

X=O, NH, NR where R is lower alkyl

Y=optionally substituted aryl or heterocyclyl.

31. (Withdrawn) The compound, according to claim 24, wherein said compound has the following structure:



n=0 to 2

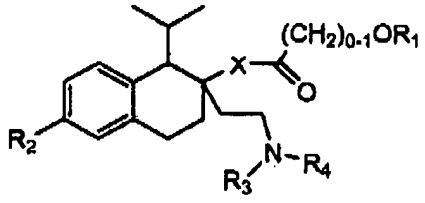
X=O, S, SO, SO_2, NH NR or $N(CH_2)_mCOOH$ where m is 0 or 2

Y=aryl or heterocyclyl substituted with $(CH_2)_mCOOH$ where m is 0 to 2.

32. (Currently Amended) The method, according to claim ~~22~~23, wherein the patient is a human.

33. (Currently Amended) The method, according to claim ~~22~~23, wherein said method is used to treat a condition selected from the group consisting of hypertension, angina, ischemia, arrhythmia, congestive heart failure, and cardiac insufficiency.

34. (New) A method for blocking a calcium channel in a patient in need of such blocking wherein said method comprises administering to said patient a calcium channel blocking compound wherein said compound has the following structure:



wherein:

X=a bond, $(CH_2)_n$, O, S, or $O(CH_2)_n$,

wherein n=1-6;

R_1=C_{1-6} alkyl, optionally substituted with OH or NH_2;

R_2=F or $COOR_5$,

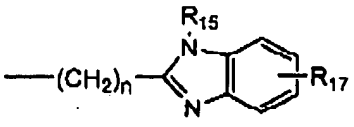
wherein R_5 is C_{1-6} alkyl, optionally substituted with OH or NH_2;

R_3=CH_3 or $(CH_2)_n$–$COOR_6$,

wherein n=1-6 and R_6 is C_{1-6} alkyl, optionally substituted with OH or NH_2;

R_4=$(CH_2)_n$–COR_7R_8, –$(CH_2)_n$–$R_{10}R_{11}$ or

PAGE 17/22 * RCVD AT 5/6/2005 4:11:55 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/24 * DNIS:2730686 * CSID:3129130002 * DURATION (mm-ss):04-50



R_7=O, NH, or NR_9,

R_8=optionally substituted aryl or heterocycle,

R_9=C_{1-6} alkyl,

R_{10}=O, S, SO, SO_2, NH, or NR_{12},

R_{11}=aryl or heterocyclyl optionally substituted with $(CH_2)_nCOOR_{14}$,

R_{12}=C_{1-6} alkyl, optionally substituted with OH or NH_2,

R_{13}=C_{1-6} alkyl, optionally substituted with OH or NH_2,

R_{14}=C_{1-6} alkyl, optionally substituted with OH or NH_2,

R_{15}= is H,

R_{17}=not present or $COOR_{18}$ wherein R_{18} is C_{1-6} alkyl, optionally substituted with OH or NH_2, and wherein n=1-6.

PAGE 18/22 * RCVD AT 5/6/2005 4:11:55 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/24 * DNIS:2730686 * CSID:3129130002 * DURATION (mm-ss):04-50